MODULATORS OF β-AMYLOID PEPTIDE AGGREGATION COMPRISING D-AMINO ACIDS

Abstract

Compounds that modulate natural β amyloid peptide aggregation are provided. The modulators of the invention comprise a peptide, preferably based on a β amyloid peptide, that is comprised entirely of D-amino acids. Preferably, the peptide comprises 3-5 D-amino acid residues and includes at least two D-amino acid residues independently selected from the group consisting of D-leucine, D-phenylalanine and D-valine. In a particularly preferred embodiment, the peptide is a retro-inverso isomer of a β amyloid peptide, preferably a retro-inverso isomer of $A\beta_{17-21}$. In certain embodiments, the peptide is modified at the amino-terminus, the carboxy-terminus, or both. Preferred amino-terminal modifying groups include cyclic, heterocyclic, polycyclic and branched alkyl groups. Preferred carboxy-terminal modifying groups include an amide group, an alkyl amide group, an aryl amide group or a hydroxy group. Pharmaceutical compositions comprising the compounds of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compounds of the invention, are also disclosed.